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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes
NEWS 23	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 24	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 25	MAR 03	FRANCEPAT now available on STN
NEWS 26	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 27	MAR 29	WPIFV now available on STN
NEWS 28	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS 29	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 09:14:50 ON 02 APR 2004

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 09:15:00 ON 02 APR 2004
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FILE COVERS 1907 - 2 Apr 2004 VOL 140 ISS 15
FILE LAST UPDATED: 1 Apr 2004 (20040401/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> "influenza virus"

	18292	"INFLUENZA"
	6	"INFLUENZAS"
	18294	"INFLUENZA" ("INFLUENZA" OR "INFLUENZAS")
	297294	"VIRUS"
	63905	"VIRUSES"
	308087	"VIRUS" ("VIRUS" OR "VIRUSES")
L1	12972	"INFLUENZA VIRUS" ("INFLUENZA"(W)"VIRUS")

=> "RNA dependent RNA polymerase"

	268120	"RNA"
	21189	"RNAS"
	272005	"RNA" ("RNA" OR "RNAS")
	887987	"DEPENDENT"
	239	"DEPENDENTS"
	888148	"DEPENDENT" ("DEPENDENT" OR "DEPENDENTS")
	268120	"RNA"
	21189	"RNAS"
	272005	"RNA" ("RNA" OR "RNAS")

```
        146338 "POLYMERASE"
          8541 "POLYMERASES"
        147630 "POLYMERASE"
                 ("POLYMERASE" OR "POLYMERASES")
L2        2194 "RNA DEPENDENT RNA POLYMERASE"
                 ("RNA"(W)"DEPENDENT"(W)"RNA"(W)"POLYMERASE")

=> L1 and L2
L3         179 L1 AND L2

=> Modification and L3
        245943 MODIFICATION
        100277 MODIFICATIONS
        330109 MODIFICATION
                 (MODIFICATION OR MODIFICATIONS)
L4           3 MODIFICATION AND L3

=> mutation and L3
        199223 MUTATION
        128426 MUTATIONS
        247317 MUTATION
                 (MUTATION OR MUTATIONS)
L5          25 MUTATION AND L3

=> ""fowl plague virus"
MISMATCHED QUOTE 'VIRUS"'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> "fowl plague virus"
          5808 "FOWL"
          1211 "FOWLS"
          6561 "FOWL"
                 ("FOWL" OR "FOWLS")
          2273 "PLAGUE"
           154 "PLAGUES"
          2419 "PLAGUE"
                 ("PLAGUE" OR "PLAGUES")
        297294 "VIRUS"
         63905 "VIRUSES"
        308087 "VIRUS"
                 ("VIRUS" OR "VIRUSES")
L6         471 "FOWL PLAGUE VIRUS"
                 ("FOWL"(W)"PLAGUE"(W)"VIRUS")

=> L6 and L2
L7          11 L6 AND L2

=> L7 and L3
L8           9 L7 AND L3

=> human and L8
       1251781 HUMAN
        314767 HUMANS
       1412231 HUMAN
                 (HUMAN OR HUMANS)
L9           1 HUMAN AND L8

=> DIS L9 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.54 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
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ACCESSION NUMBER: 2002:634334 CAPLUS
DOCUMENT NUMBER: 137:180775
TITLE: **Influenza viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of **fowl plague virus** and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
PATENT ASSIGNEE(S): Artemis Pharmaceuticals Gmbh, Germany
SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233059	A1	20020821	EP 2001-103060	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002064757	A2	20020822	WO 2002-EP1257	20020207
WO 2002064757	A3	20021205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368459	A2	20031210	EP 2002-716735	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003099670	A1	20030529	US 2002-73377	20020208

PRIORITY APPLN. INFO.:
EP 2001-103060 A 20010209
US 2001-270135P P 20010220
WO 2002-EP1257 W 20020207

ABSTRACT:
The present invention provides **human influenza** ***viruses*** comprising an RNA sequence encoding a modified RNA-polymerase (RNAP). It was found that specific modifications of the RNA sequence encoding the RNAP, in particular the RNAP PB1 subunit - so as to code for a polypeptide having a higher similarity with **fowl plague virus** strain Bratislava (FPV) RNAP - provides viruses capable of recognition of viral RNA (vRNA) promoter sequence variations (the so called promoter-up variants) leading to an increase in transcription and/or replication initiation rates. The vRNA promoter may comprise the modifications G3A and C8U, or G3C and C8G, preferably G3A, U5C and C8U, or G3C, U5C and C8G in the 3'-terminal region (5'-CCUGUUUCUACU-3' or 5'-CCUGUUUUUACU-3'); and the modifications U3A and A8U in the 5'-terminal region (5'-AGAAGAAUCAAGG-3'). The present invention also provides a process for the preparation thereof, pharmaceutical compns. comprising said **human influenza viruses** and their use for gene transfer into mammalian cells, for ex vivo gene transfer into antigen-presenting cells, such as dendritic cells, for in vivo somatic gene therapy, or in vivo vaccination purposes. The invention also relates to other non-avian **influenza viruses**, including equine, porcine ***influenza*** **viruses**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> DIS L8 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 22.87 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L8 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:634334 CAPLUS
DOCUMENT NUMBER: 137:180775
TITLE: **Influenza viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of **fowl plague virus** and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
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SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
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WO 2002064757	A2	20020822	WO 2002-EP1257	20020207
WO 2002064757	A3	20021205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368459	A2	20031210	EP 2002-716735	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003099670	A1	20030529	US 2002-73377	20020208

PRIORITY APPLN. INFO.:
EP 2001-103060 A 20010209
US 2001-270135P P 20010220
WO 2002-EP1257 W 20020207

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influenza **viruses**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:494975 CAPLUS
DOCUMENT NUMBER: 95:94975
TITLE: Nuclear and cytoplasmic distribution of **influenza virus** P polypeptides in infected BHK-21 cells
AUTHOR(S): Conti, G.; Natali, A.; Portincasa, P.; Schito, G. C.
CORPORATE SOURCE: Ist. Microbiol., Univ. Studi Parma, Parma, Italy
SOURCE: Microbiologica (1981), 4(3), 339-45
CODEN: MIBLDR; ISSN: 0391-5352
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In baby hamster kidney (BHK-21) cells infected with Dobson strain, influenza A-***fowl*** **plague virus**, the 3 high-mol.-weight P proteins associated with the viral **RNA-dependent RNA** ***polymerase*** was distributed differently between nucleus and cytoplasm. Dobson P1 and P3 polypeptides migrated to the cell nucleus immediately after infection initiation, indicating these polypeptides are involved in complementary RNA synthesis. P2 was mainly associated with the cytoplasm of infected cells and thus may function in viral RNA synthesis.

L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:581917 CAPLUS
DOCUMENT NUMBER: 87:181917
TITLE: RNA polymerase activities of nuclei from **influenza virus**-infected cells
AUTHOR(S): Mahy, Brian W. J.; Hastie, Nicholas D.; Raper, Robert H.; Brownson, Jennifer M. T.; Carroll, Anthony R.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Negat. Strand Viruses, Pap. Symp. (1975), Meeting Date 1973, Volume 1, 445-67. Editor(s): Mahy, Brian W. J.; Barry, Richard D. Academic: London, Engl.
CODEN: 36LUAU
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
RNA formation was inhibited by α-amanitin in the nuclei of cells infected with influenza (**fowl plague**), **virus**, but not in uninfected cells. RNA polymerase II activity in **influenza** ***virus*** -infected cells was increased and the increase corresponded with the 1st 2 periods of increased RNA formation. A new **RNA-** ***dependent*** **RNA polymerase** which was α-amanitin- and actinomycin D-insensitive, and synthesized both complementary RNA and viral RNA in an in vitro system was induced in virus-infected cells. This enzyme activity was contained within infected cell nuclei and was not due to cytoplasmic contamination, but could not be distinguished from the microsomal **RNA-dependent RNA** ***polymerase*** on the basis of pH or divalent cation requirements.

L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:566048 CAPLUS
DOCUMENT NUMBER: 81:166048
TITLE: Topography of RNA synthesis in cells infected with **fowl plague virus**
AUTHOR(S): Armstrong, Sylvia J.; Barry, R. D.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK

SOURCE: Journal of General Virology (1974), 24, Pt. 3, 535-47
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The site of **influenza virus**-induced RNA synthesis in infected chick embryo cells was determined by autoradiog. Following 5 min pulses of uridine-3H, 2 distinguishable phases of induced RNA synthesis were detected by grain counting in the nucleus, both of which occurred predominantly in the neoplasm. Cytoplasmic RNA synthesis was not detected in **fowl** ***plague*** **virus** (FPV)-infected cells; a significant increase in cytoplasmic grain count was detected in Newcastle disease virus infected cells from 4-8 hr after infection. Cordycepin (3'-deoxyadenosine) inhibited nucleolar RNA synthesis in chicken embryo fibroblasts (CEF) to a greater extent than nucleoplasmic RNA synthesis; FPV-induced RNA synthesis in cordycepin-treated cells occurred in the nucleoplasm. Treatment of FPV-infected cells with α-amanitin inhibited the 1st peak of virus-induced nucleoplasmic RNA synthesis. Fixed prepns. of whole FPV-infected cells were incubated with an **RNA-dependent RNA** ***polymerase*** reaction mixture and examined by autoradiog. A peak of enzyme activity was detected at 3 hr after infection in the nucleoplasm; a 2nd peak of activity was detected at 6 hr after infection and was wholly cytoplasmic. Thus, RNA synthesis in vivo in cells infected with **influenza** ***viruses*** occurs in the cell nucleus and the increased level of nucleoplasmic RNA synthesis at .apprx. 1 hr after infection signifies increased transcription of cell DNA. Apparently, the microsomal **RNA-** ***dependent*** **RNA polymerase** found in FPV-infected cells does not function in vivo.

L8 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:1956 CAPLUS
DOCUMENT NUMBER: 80:1956
TITLE: **RNA-dependent RNA** **polymerase** in nuclei of cells infected with **influenza virus**
AUTHOR(S): Hastie, N. D.; Mahy, B. W. J.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Journal of Virology (1973), 12(5), 951-61
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Nuclei purified from chicken embryo fibroblast cells infected with influenza (***fowl*** **plague**) **virus** contain an **RNA-** ***dependent*** **RNA polymerase**. The in vitro activity of this enzyme is insensitive to actinomycin A and is completely destroyed by preincubation with RNase. Enzyme induction is prevented if cells are treated with actinomycin D or cycloheximide at the time of infection. **RNA-** ***dependent*** **RNA polymerase** activity increases rapidly in cell nuclei from 1 hr postinfection, reaches a maximum at 3 to 4 hr, then declines. A similar RNA polymerase activity in the microsomal cell fraction increases from 2 hr postinfection and reaches a maximum at 5 to 6 hr. The characteristics of the nuclear and microsomal enzymes in vitro are similar with respect to pH and divalent cation requirements. The in vitro products of enzyme activity present in the nuclear and microsomal fractions of cells infected for 3 and 5 hr were characterized by sucrose d. gradient anal. and annealing to virion RNA. The microsomal RNA polymerase product contained 67 and 93% RNA complementary to virion RNA at 3 and 5 hr, resp. For the nuclear RNA polymerase product these values were 40% in each case.

L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:69914 CAPLUS

DOCUMENT NUMBER: 76:69914
TITLE: Replication of **fowl plague virus** RNA
AUTHOR(S): Mahy, B. W. J.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Biol. Large RNA Viruses, Pap. Symp. (1970), Meeting Date 1969, 392-415. Editor(s): Barry, Richard D. Academic: London, Engl.
CODEN: 24FAAH
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
Three distinct RNA polymerase activities were associated with cells infected with fowl pest virus. A transitory increase in host cell DNA-dependent RNA polymerase activity occurred in the nucleus early in infection, followed by the appearance of **RNA-dependent RNA** ***polymerases*** in both nucleus and microsomal fraction. The latter enzyme synthesized in vitro a mixture of single- and double-stranded RNA, the former sedimenting mainly in the 8 S region on sucrose d. gradients with a small fraction in the 18 S region, the pattern corresponding closely with either late yield virus RNA or von Magnus virus RNA. The double-stranded RNA sedimented at 12 S, although replicative intermediate types sedimenting at 14-20 S were also detectable. Similar RNA species were detectable in vivo by pulse-labeling influenza-infected cells at the time of polymerase harvest, but with the various RNA species in different proportions, most of the RNA sedimenting at 18 S with a small fraction at 8 S. A 12 S double-stranded RNA was also synthesized in vivo, but in much smaller amts. than in vitro. Pulse-chase anal. of the double-stranded RNA synthesized in vitro showed that most of it was stable, with only a small portion turning over during the reaction. The RNA formed by the microsomal RNA polymerase in vitro hybridized with both RNA present in infected cell microsomes and RNA from mature virus, indicating that a proportion of the RNA thus formed was complementary to virus RNA.

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:51703 CAPLUS
DOCUMENT NUMBER: 74:51703
TITLE: Inhibition of influenza RNA polymerase by specific antiserum
AUTHOR(S): Scholtissek, Christoph; Becht, Hermann; Rott, Rudolf
CORPORATE SOURCE: Inst. Virol., Justus Liebig-Univ., Giessen, Fed. Rep. Ger.
SOURCE: Virology (1971), 43(1), 137-43
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The **RNA-dependent RNA-polymerases** induced by all influenza A viruses tested can be inhibited specifically by immune serum of a chicken infected with **fowl plague** ***virus.*** The corresponding polymerases of influenza B Lee and of Newcastle disease virus cannot be inhibited by the fowl plague convalescent serum. Antibodies against ribonucleoprotein-antigen and envelope components or a direct action of RNase are not responsible for the inhibition. The results are consistent with the view that at least part of the **influenza** ***virus*** -induced RNA polymerase is coded by the viral genome, and is expressed as a common antigenic determinant within the influenza A group.

L8 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1969:400981 CAPLUS
DOCUMENT NUMBER: 71:981
TITLE: Synthesis in vitro of RNA complementary to parental viral RNA by RNA polymerase induced by

influenza virus
AUTHOR(S): Scholtissek, Christoph
CORPORATE SOURCE: Justus Liebig-Univ., Giessen, Fed. Rep. Ger.
SOURCE: Biochimica et Biophysica Acta (1969), 179(2), 389-97
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
After infection of chick fibroblasts in culture with **fowl** ***plague*** **virus** (influenza A) the synthesis of an **RNA**-***dependent*** **RNA polymerase** was induced. In vitro the enzyme synthesized between 85 and 100% of RNA with a base sequence complementary to the parental viral RNA as shown by hybridization expts. and nearest-neighbor anal. The product formed in vitro was mainly single-stranded RNA.

L8 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:53071 CAPLUS
DOCUMENT NUMBER: 66:53071
TITLE: Failure of function of the "early protein" induced by an **influenza virus** in cells infected by Newcastle disease virus
AUTHOR(S): Scholtissek, Christoph; Rott, Rudolf
CORPORATE SOURCE: Univ. Giessen, Giessen, Fed. Rep. Ger.
SOURCE: Nature (London, United Kingdom) (1967), 213(5072), 186
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
After infection of chick embryo cells with **fowl plague** ***virus*** (FPV), an influenza A virus, or with Newcastle disease virus (NDV), a parainfluenza virus, "early proteins" are synthesized before viral RNA synthesis starts. In the present study, the "early proteins" induced by FPV were not able to function for the multiplication of NDV in chick embryo cells in culture. It had previously been established that FPV RNA is synthesized within the cell nucleus, while RNA probably replicates in the cytoplasm. Thus, the "early proteins" of FPV might not be able to leave the nucleus and consequently fail to function for the multiplication of NDV. As already shown with 2 different RNA-containing phages, the **RNA-dependent** ***RNA*** **polymerase** is very specific in the sense that it uses only that RNA as template which has induced its synthesis. A similar situation might apply to different myxoviruses.

=> DIS L7 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 27.95 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L7 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:634334 CAPLUS
DOCUMENT NUMBER: 137:180775
TITLE: Influenza viruses with enhanced transcription and replication capacities comprising RNA polymerase similar to that of **fowl plague** **virus** and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
PATENT ASSIGNEE(S): Artemis Pharmaceuticals Gmbh, Germany
SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233059	A1	20020821	EP 2001-103060	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368459	A2	20031210	EP 2002-716735	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003099670	A1	20030529	US 2002-73377	20020208

PRIORITY APPLN. INFO.:
EP 2001-103060 A 20010209
US 2001-270135P P 20010220
WO 2002-EP1257 W 20020207

ABSTRACT:
The present invention provides human influenza viruses comprising an RNA sequence encoding a modified RNA-polymerase (RNAP). It was found that specific modifications of the RNA sequence encoding the RNAP, in particular the RNAP PB1 subunit - so as to code for a polypeptide having a higher similarity with ***fowl*** **plague virus** strain Bratislava (FPV) RNAP - provides viruses capable of recognition of viral RNA (vRNA) promoter sequence variations (the so called promoter-up variants) leading to an increase in transcription and/or replication initiation rates. The vRNA promoter may comprise the modifications G3A and C8U, or G3C and C8G, preferably G3A, U5C and C8U, or G3C, U5C and C8G in the 3'-terminal region (5'-CCUGUUUCUACU-3' or 5'-CCUGUUUUUACU-3'); and the modifications U3A and A8U in the 5'-terminal region (5'-AGAAGAAUCAAGG-3'). The present invention also provides a process for the preparation thereof, pharmaceutical compns. comprising said human influenza viruses and their use for gene transfer into mammalian cells, for ex vivo gene transfer into antigen-presenting cells, such as dendritic cells, for in vivo somatic gene therapy, or in vivo vaccination purposes. The invention also relates to other non-avian influenza viruses, including equine, porcine influenza viruses.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:494975 CAPLUS
DOCUMENT NUMBER: 95:94975
TITLE: Nuclear and cytoplasmic distribution of influenza virus P polypeptides in infected BHK-21 cells
AUTHOR(S): Conti, G.; Natali, A.; Portincasa, P.; Schito, G. C.
CORPORATE SOURCE: Ist. Microbiol., Univ. Studi Parma, Parma, Italy
SOURCE: Microbiologica (1981), 4(3), 339-45
CODEN: MIBLDR; ISSN: 0391-5352
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In baby hamster kidney (BHK-21) cells infected with Dobson strain, influenza A-***fowl*** **plague virus**, the 3 high-mol.-weight P proteins

associated with the viral **RNA-dependent RNA** ***polymerase*** was distributed differently between nucleus and cytoplasm. Dobson P1 and P3 polypeptides migrated to the cell nucleus immediately after infection initiation, indicating these polypeptides are involved in complementary RNA synthesis. P2 was mainly associated with the cytoplasm of infected cells and thus may function in viral RNA synthesis.

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:581917 CAPLUS
DOCUMENT NUMBER: 87:181917
TITLE: RNA polymerase activities of nuclei from influenza virus-infected cells
AUTHOR(S): Mahy, Brian W. J.; Hastie, Nicholas D.; Raper, Robert H.; Brownson, Jennifer M. T.; Carroll, Anthony R.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Negat. Strand Viruses, Pap. Symp. (1975), Meeting Date 1973, Volume 1, 445-67. Editor(s): Mahy, Brian W. J.; Barry, Richard D. Academic: London, Engl.
CODEN: 36LUAU
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
RNA formation was inhibited by α-amanitin in the nuclei of cells infected with influenza (**fowl plague**), **virus**, but not in uninfected cells. RNA polymerase II activity in influenza virus-infected cells was increased and the increase corresponded with the 1st 2 periods of increased RNA formation. A new **RNA-dependent RNA** ***polymerase*** which was α-amanitin- and actinomycin D-insensitive, and synthesized both complementary RNA and viral RNA in an in vitro system was induced in virus-infected cells. This enzyme activity was contained within infected cell nuclei and was not due to cytoplasmic contamination, but could not be distinguished from the microsomal **RNA-dependent** ***RNA*** **polymerase** on the basis of pH or divalent cation requirements.

L7 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1976:537950 CAPLUS
DOCUMENT NUMBER: 85:137950
TITLE: Effect of adamantane derivatives on the activity of orthomyxovirus **RNA-dependent RNA polymerase**
AUTHOR(S): Kalnina, V.; Indulena, M.
CORPORATE SOURCE: A. Kirhensteins Inst. Microbiol., Riga, USSR
SOURCE: Acta Virologica (English Edition) (1976), 20(4), 343-6
CODEN: AVIRA2; ISSN: 0001-723X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The virion-associated **RNA-dependent RNA** ***polymerase*** [9026-28-2] activities from **fowl plague** ***virus*** and influenza B virus were inhibited by a number of adamantane derivs. The ability of a compound to inhibit RNA polymerase in vitro correlated with its previously demonstrated capacity to suppress virus reproduction in vivo. Therefore, the antiviral activities of the adamantane derivs. apparently involve an inhibition of virus genome transcription directed by the virion-associated transcriptase.

L7 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:566048 CAPLUS
DOCUMENT NUMBER: 81:166048
TITLE: Topography of RNA synthesis in cells infected with

fowl plague virus
AUTHOR(S): Armstrong, Sylvia J.; Barry, R. D.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Journal of General Virology (1974), 24, Pt. 3, 535-47
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The site of influenza virus-induced RNA synthesis in infected chick embryo cells was determined by autoradiog. Following 5 min pulses of uridine-3H, 2 distinguishable phases of induced RNA synthesis were detected by grain counting in the nucleus, both of which occurred predominantly in the neoplasm. Cytoplasmic RNA synthesis was not detected in **fowl plague** ***virus*** (FPV)-infected cells; a significant increase in cytoplasmic grain count was detected in Newcastle disease virus infected cells from 4-8 hr after infection. Cordycepin (3'-deoxyadenosine) inhibited nucleolar RNA synthesis in chicken embryo fibroblasts (CEF) to a greater extent than nucleoplasmic RNA synthesis; FPV-induced RNA synthesis in cordycepin-treated cells occurred in the nucleoplasm. Treatment of FPV-infected cells with α-amanitin inhibited the 1st peak of virus-induced nucleoplasmic RNA synthesis. Fixed prepns. of whole FPV-infected cells were incubated with an **RNA-** ***dependent*** **RNA polymerase** reaction mixture and examined by autoradiog. A peak of enzyme activity was detected at 3 hr after infection in the nucleoplasm; a 2nd peak of activity was detected at 6 hr after infection and was wholly cytoplasmic. Thus, RNA synthesis in vivo in cells infected with influenza viruses occurs in the cell nucleus and the increased level of nucleoplasmic RNA synthesis at .apprx. 1 hr after infection signifies increased transcription of cell DNA. Apparently, the microsomal **RNA-** ***dependent*** **RNA polymerase** found in FPV-infected cells does not function in vivo.

L7 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1974:1956 CAPLUS
DOCUMENT NUMBER: 80:1956
TITLE: **RNA-dependent RNA polymerase** in nuclei of cells infected with influenza virus
AUTHOR(S): Hastie, N. D.; Mahy, B. W. J.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Journal of Virology (1973), 12(5), 951-61
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Nuclei purified from chicken embryo fibroblast cells infected with influenza (***fowl*** **plague**) **virus** contain an **RNA-** ***dependent*** **RNA polymerase**. The in vitro activity of this enzyme is insensitive to actinomycin A and is completely destroyed by preincubation with RNase. Enzyme induction is prevented if cells are treated with actinomycin D or cycloheximide at the time of infection. **RNA-** ***dependent*** **RNA polymerase** activity increases rapidly in cell nuclei from 1 hr postinfection, reaches a maximum at 3 to 4 hr, then declines. A similar RNA polymerase activity in the microsomal cell fraction increases from 2 hr postinfection and reaches a maximum at 5 to 6 hr. The characteristics of the nuclear and microsomal enzymes in vitro are similar with respect to pH and divalent cation requirements. The in vitro products of enzyme activity present in the nuclear and microsomal fractions of cells infected for 3 and 5 hr were characterized by sucrose d. gradient anal. and annealing to virion RNA. The microsomal RNA polymerase product contained 67 and 93% RNA complementary to virion RNA at 3 and 5 hr, resp. For the nuclear RNA polymerase product these values were 40% in each case.

L7 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:69914 CAPLUS
DOCUMENT NUMBER: 76:69914
TITLE: Replication of **fowl plague virus** RNA
AUTHOR(S): Mahy, B. W. J.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Biol. Large RNA Viruses, Pap. Symp. (1970), Meeting Date 1969, 392-415. Editor(s): Barry, Richard D. Academic: London, Engl.
CODEN: 24FAAH
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
Three distinct RNA polymerase activities were associated with cells infected with fowl pest virus. A transitory increase in host cell DNA-dependent RNA polymerase activity occurred in the nucleus early in infection, followed by the appearance of **RNA-dependent RNA** ***polymerases*** in both nucleus and microsomal fraction. The latter enzyme synthesized in vitro a mixture of single- and double-stranded RNA, the former sedimenting mainly in the 8 S region on sucrose d. gradients with a small fraction in the 18 S region, the pattern corresponding closely with either late yield virus RNA or von Magnus virus RNA. The double-stranded RNA sedimented at 12 S, although replicative intermediate types sedimenting at 14-20 S were also detectable. Similar RNA species were detectable in vivo by pulse-labeling influenza-infected cells at the time of polymerase harvest, but with the various RNA species in different proportions, most of the RNA sedimenting at 18 S with a small fraction at 8 S. A 12 S double-stranded RNA was also synthesized in vivo, but in much smaller amts. than in vitro. Pulse-chase anal. of the double-stranded RNA synthesized in vitro showed that most of it was stable, with only a small portion turning over during the reaction. The RNA formed by the microsomal RNA polymerase in vitro hybridized with both RNA present in infected cell microsomes and RNA from mature virus, indicating that a proportion of the RNA thus formed was complementary to virus RNA.

L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:51703 CAPLUS
DOCUMENT NUMBER: 74:51703
TITLE: Inhibition of influenza RNA polymerase by specific antiserum
AUTHOR(S): Scholtissek, Christoph; Becht, Hermann; Rott, Rudolf
CORPORATE SOURCE: Inst. Virol., Justus Liebig-Univ., Giessen, Fed. Rep. Ger.
SOURCE: Virology (1971), 43(1), 137-43
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The **RNA-dependent RNA-polymerases** induced by all influenza A viruses tested can be inhibited specifically by immune serum of a chicken infected with **fowl plague** ***virus.*** The corresponding polymerases of influenza B Lee and of Newcastle disease virus cannot be inhibited by the fowl plague convalescent serum. Antibodies against ribonucleoprotein-antigen and envelope components or a direct action of RNase are not responsible for the inhibition. The results are consistent with the view that at least part of the influenza virus-induced RNA polymerase is coded by the viral genome, and is expressed as a common antigenic determinant within the influenza A group.

L7 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1970:497218 CAPLUS
DOCUMENT NUMBER: 73:97218

TITLE: Effect of mithramycin on the multiplication of myxoviruses
AUTHOR(S): Scholtissek, Christoph; Becht, Hermann; Macpherson, I.
CORPORATE SOURCE: Inst. Virol., Justus Liebig-Univ., Giessen, Fed. Rep. Ger.
SOURCE: Journal of General Virology (1970), 8(Pt. 1), 11-19
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Mithramycin inhibited RNA synthesis in chick embryo cells in culture almost as efficiently as actinomycin D, although inhibition was considerably delayed. There was no direct effect on cellular protein synthesis. Mithramycin interfered with the multiplication of **fowl plague** ***virus*** (influenza A) but had little effect on the multiplication of Newcastle disease virus (parainfluenza). Ten μg/ml of mithramycin, when added immediately after infection, preferentially inhibited the synthesis of fowl plague minus strand RNA in culture, but it had only a slight effect on the production of plus strand RNA. The synthesis of virus **RNA**-***dependent*** **RNA polymerase** and RNP-antigen was only slightly inhibited, while the production of hemagglutinin and neuraminidase was strongly affected.

L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1969:400981 CAPLUS
DOCUMENT NUMBER: 71:981
TITLE: Synthesis in vitro of RNA complementary to parental viral RNA by RNA polymerase induced by influenza virus
AUTHOR(S): Scholtissek, Christoph
CORPORATE SOURCE: Justus Liebig-Univ., Giessen, Fed. Rep. Ger.
SOURCE: Biochimica et Biophysica Acta (1969), 179(2), 389-97
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
After infection of chick fibroblasts in culture with **fowl** ***plague*** **virus** (influenza A) the synthesis of an **RNA**-***dependent*** **RNA polymerase** was induced. In vitro the enzyme synthesized between 85 and 100% of RNA with a base sequence complementary to the parental viral RNA as shown by hybridization expts. and nearest-neighbor anal. The product formed in vitro was mainly single-stranded RNA.

L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:53071 CAPLUS
DOCUMENT NUMBER: 66:53071
TITLE: Failure of function of the "early protein" induced by an influenza virus in cells infected by Newcastle disease virus
AUTHOR(S): Scholtissek, Christoph; Rott, Rudolf
CORPORATE SOURCE: Univ. Giessen, Giessen, Fed. Rep. Ger.
SOURCE: Nature (London, United Kingdom) (1967), 213(5072), 186
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
After infection of chick embryo cells with **fowl plague** ***virus*** (FPV), an influenza A virus, or with Newcastle disease virus (NDV), a parainfluenza virus, "early proteins" are synthesized before viral RNA synthesis starts. In the present study, the "early proteins" induced by FPV were not able to function for the multiplication of NDV in chick embryo cells in culture. It had previously been established that FPV RNA is synthesized

within the cell nucleus, while RNA probably replicates in the cytoplasm. Thus, the "early proteins" of FPV might not be able to leave the nucleus and consequently fail to function for the multiplication of NDV. As already shown with 2 different RNA-containing phages, the **RNA-dependent** ***RNA*** **polymerase** is very specific in the sense that it uses only that RNA as template which has induced its synthesis. A similar situation might apply to different myxoviruses.

=> DIS L5 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 25 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 63.53 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L5 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:176523 CAPLUS
DOCUMENT NUMBER: 140:234378
TITLE: Production of recombinant respiratory syncytial viruses (RSVs) with chimeric genome or antigenome, expressing immunomodulators, and uses as infectious attenuated RSV vaccine
INVENTOR(S): Collins, Peter L.; Bukreyev, Alexander; Murphy, Brian P.; Whitehead, Stephen S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 291,894.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6699476	B1	20040302	US 2000-614285	20000712
CN 1224462	A	19990728	CN 1997-196139	19970715
US 5993824	A	19991130	US 1997-892403	19970715
US 6689367	B1	20040210	US 1999-291894	19990413

PRIORITY APPLN. INFO.:

US 1996-21773P	P	19960715
US 1997-46141P	P	19970509
US 1997-47634P	P	19970523
US 1997-892403	A2	19970715
US 1999-291894	A2	19990413
US 1999-143425P	P	19990713
US 1995-7083P	P	19950927
US 1996-720132	A2	19960927

ABSTRACT:
Recombinant respiratory syncytial virus (RSV) are provided which express one or more immune modulatory mols. The recombinant virus is modified by addition or substitution of a polynucleotide sequence encoding the immune modulatory mol., which is preferably a cytokine. Introduction of the cytokine increase, decrease, or otherwise enhances aspects of viral biol. and/or host immune responses to RSV to facilitate vaccine use of the virus. Cytokines for use within the invention include but are not limited to interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 5 (IL-5), interleukin 6 (IL6), or interleukin 18 (IL-18), tumor necrosis factor (TNF) alpha, interferon gamma (IFN), and granulocyte-macrophage colony stimulating factor (GM-CSF). The polynucleotide or immune modulatory mol. is preferably added or substituted into the recombinant viral genome or antigenome, typically at an intergenic or other non-coding site, as a sep. gene but may be otherwise expressed, for example as a fusion protein.

REFERENCE COUNT: 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L5 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:367730 CAPLUS
DOCUMENT NUMBER: 139:176433
TITLE: Threonine 157 of **influenza virus** PA polymerase subunit modulates RNA replication in infectious viruses
AUTHOR(S): Huarte, Maite; Falcon, Ana; Nakaya, Yuri; Ortin, Juan; Garcia-Sastre, Adolfo; Nieto, Amelia
CORPORATE SOURCE: Centro Nacional de Biotecnologia, Cantoblanco, Madrid, 28049, Spain
SOURCE: Journal of Virology (2003), 77(10), 6007-6013
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Previous results have shown a correlation between the decrease in protease activity of several influenza A virus PA protein mutants and the capacity to replicate of the corresponding mutant ribonucleoproteins (RNPs) reconstituted in vivo. In this work we studied the phenotype of mutant viruses containing these ***mutations.*** Viruses with a T162A **mutation**, which showed a very moderate decrease both in protease and replication activities of reconstituted RNPs, showed a wild-type phenotype. Viruses with a T157A ***mutation*** , which presented a severe decrease in protease activity and replication of RNPs, showed a complex phenotype: (i) transport to the nucleus of PAT157A protein was delayed, (ii) virus multiplication was reduced at both low and high multiplicities, (iii) transcriptive synthesis was unaltered while replicative synthesis, especially cRNA, was diminished, and (iv) viral pathogenesis in mice was reduced, as measured by loss of body weight and virus titers in lungs. Finally, recombinant viruses with a T157E **mutation** in PA protein, which resulted in a drastic reduction of protease and replication activities of RNPs, were not viable. These results indicate that residue T157 in PA protein is important for the capacity of viral polymerase to synthesize cRNA.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:330669 CAPLUS
DOCUMENT NUMBER: 139:227164
TITLE: Characterization of a swine-like reassortant H1N2 **influenza virus** isolated from a wild duck in the United States
AUTHOR(S): Olsen, Christopher W.; Karasin, Alexander; Erickson, Gene
CORPORATE SOURCE: School of Veterinary Medicine, Department of Pathobiological Sciences, University of Wisconsin-Madison, Madison, WI, 53717, USA
SOURCE: Virus Research (2003), 93(1), 115-121
CODEN: VIREDF; ISSN: 0168-1702
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
An H1N2 **influenza virus** (A/Duck/North Carolina/91347/01) (Dk/NC) was isolated from a wild duck in the United States in 2001. Genetic analyses showed that this duck virus has the same human/classical swine/avian reassortant genotype as the H1N2 viruses that have been isolated from pigs and turkeys in the US since 1999. Phylogenetic analyses of each gene segment further confirmed that the Dk/NC virus is closely related to the domestic animal H1N2 isolates. In particular, Dk/NC is most closely related to a swine H1N2 virus also isolated in North Carolina. These two viruses and a

phylogenetically-defined subset of addnl. swine H1N2 viruses share a common ***mutation*** in the Sb antigenic site on the hemagglutinin protein. The recovery of Dk/NC from a wild bird raises concerns for further widespread distribution of these H1N2 viruses via waterfowl migration.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:199024 CAPLUS
DOCUMENT NUMBER: 138:396975
TITLE: Neurovirulence in mice of H5N1 **influenza virus** genotypes isolated from Hong Kong poultry in 2001
AUTHOR(S): Lipatov, Aleksandr S.; Krauss, Scott; Guan, Yi; Peiris, Malik; Rehg, Jerold E.; Perez, Daniel R.; Webster, Robert G.
CORPORATE SOURCE: Division of Virology, Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA
SOURCE: Journal of Virology (2003), 77(6), 3816-3823
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
We studied the pathogenicity of five different genotypes (A to E) of highly pathogenic avian H5N1 viruses, which contained HA genes similar to those of the H5N1 virus A/goose/Guangdong/1/96 and five different combinations of "internal" genes, in a mouse model. Highly pathogenic, neurotropic variants of genotypes A, C, D, and E were isolated from the brain after a single intranasal passage in mice. Genotype B virus was isolated from lungs only. The mouse brain variants had amino acid changes in all gene products except PB1, NP, and NS1 proteins but no common sets of **mutations**. We conclude that the original H5N1/01 isolates of genotypes A, C, D, and E were heterogeneous and that highly pathogenic neurotropic variants can be rapidly selected in mice.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:187404 CAPLUS
DOCUMENT NUMBER: 138:332801
TITLE: Alternative base pairs attenuate influenza a virus when introduced into the duplex region of the conserved viral RNA promoter of either the NS or the PA gene
AUTHOR(S): Catchpole, A. P.; Mingay, L. J.; Fodor, E.; Brownlee, G. G.
CORPORATE SOURCE: Sir William Dunn School of Pathology, Chemical Pathology Unit, University of Oxford, Oxford, OX1 3RE, UK
SOURCE: Journal of General Virology (2003), 84(3), 507-515
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The development of plasmid-based rescue systems for **influenza** ***virus*** has allowed previous studies of the neuraminidase (NA) virion RNA (vRNA) promoter to be extended, to test the hypothesis that alternative base pairs in the conserved **influenza virus** vRNA promoter cause attenuation when introduced into other gene segments. Influenza A/WSN/33 viruses with alternative base pairs in the duplex region of the vRNA promoter

of either the polymerase acidic (PA) or the NS (non-structural 1, NS1, and nuclear export, NEP, -encoding) gene have been rescued. Virus growth in MDBK cells demonstrated that one of the **mutations**, the D2 **mutation** (U-A replacing G-C at nucleotide positions 12'-11), caused significant virus attenuation when introduced into either the PA or the NS gene. The D2 ***mutation*** resulted in the reduction of PA- or NS-specific vRNA and mRNA levels in PA- or NS-recombinant viruses, resp. Since the D2 **mutation** attenuates **influenza virus** when introduced into either the PA or the NS gene segments, or the NA gene segment, as demonstrated previously, this suggests that this **mutation** will lead to virus attenuation when introduced into any of the eight gene segments. Such a **mutation** may be useful in the prodn. of live-attenuated viruses.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:674028 CAPLUS
DOCUMENT NUMBER: 137:365475
TITLE: A single amino acid **mutation** in the PA subunit of the **influenza virus** RNA polymerase inhibits endonucleolytic cleavage of capped RNAs
AUTHOR(S): Fodor, Ervin; Crow, Mandy; Mingay, Louise J.; Deng, Tao; Sharps, Jane; Fechter, Pierre; Brownlee, George G.
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of Oxford, Oxford, OX1 3RE, UK
SOURCE: Journal of Virology (2002), 76(18), 8989-9001
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The influenza A virus **RNA-dependent RNA** ***polymerase*** consists of three subunits-PB1, PB2, and PA. The PB1 subunit is the catalytically active polymerase, catalyzing the sequential addition of nucleotides to the growing RNA chain. The PB2 subunit is a cap-binding protein that plays a role in initiation of viral mRNA synthesis by recruiting capped RNA primers. The function of PA is unknown, but previous studies of temperature-sensitive viruses with **mutations** in PA have implied a role in viral RNA replication. In this report we demonstrate that the PA subunit is required not only for replication but also for transcription of viral RNA. We mutated evolutionarily conserved amino acids to alanines in the C-terminal region of the PA protein, since the C-terminal region shows the highest degree of conservation between PA proteins of influenza A, B, and C viruses. We tested the effects of these **mutations** on the ability of RNA polymerase to transcribe and replicate viral RNA. We also tested the compatibility of these **mutations** with viral viability by using reverse-genetics techniques. A mutant with a histidine-to-alanine change at position 510 (H510A) in the PA protein of influenza A/WSN/33 virus showed a differential effect on transcription and replication. This mutant was able to perform replication (vRNA→cRNA→vRNA), but its transcriptional activity (vRNA→mRNA) was negligible. In vitro analyses of the H510A recombinant polymerase, by using transcription initiation, vRNA-binding, capped-RNA-binding, and endonuclease assays, suggest that the primary defect of this mutant polymerase is in its endonuclease activity.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:634334 CAPLUS
DOCUMENT NUMBER: 137:180775

TITLE: **Influenza viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of fowl plague virus and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
PATENT ASSIGNEE(S): Artemis Pharmaceuticals Gmbh, Germany
SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233059	A1	20020821	EP 2001-103060	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002064757	A2	20020822	WO 2002-EP1257	20020207
WO 2002064757	A3	20021205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368459	A2	20031210	EP 2002-716735	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003099670	A1	20030529	US 2002-73377	20020208

PRIORITY APPLN. INFO.:
EP 2001-103060 A 20010209
US 2001-270135P P 20010220
WO 2002-EP1257 W 20020207

ABSTRACT:
The present invention provides human **influenza viruses** comprising an RNA sequence encoding a modified RNA-polymerase (RNAP). It was found that specific modifications of the RNA sequence encoding the RNAP, in particular the RNAP PB1 subunit - so as to code for a polypeptide having a higher similarity with fowl plague virus strain Bratislava (FPV) RNAP - provides viruses capable of recognition of viral RNA (vRNA) promoter sequence variations (the so called promoter-up variants) leading to an increase in transcription and/or replication initiation rates. The vRNA promoter may comprise the modifications G3A and C8U, or G3C and C8G, preferably G3A, U5C and C8U, or G3C, U5C and C8G in the 3'-terminal region (5'-CCUGUUUCUACU-3' or 5'-CCUGUUUUUACU-3'); and the modifications U3A and A8U in the 5'-terminal region (5'-AGAAGAAUCAAGG-3'). The present invention also provides a process for the preparation thereof, pharmaceutical compns. comprising said human ***influenza*** **viruses** and their use for gene transfer into mammalian cells, for ex vivo gene transfer into antigen-presenting cells, such as dendritic cells, for in vivo somatic gene therapy, or in vivo vaccination purposes. The invention also relates to other non-avian **influenza** ***viruses*** , including equine, porcine **influenza viruses**
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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:613078 CAPLUS
DOCUMENT NUMBER: 135:329013
TITLE: Functional analysis of PA binding by influenza A virus

PB1: effects on polymerase activity and viral infectivity

AUTHOR(S): Perez, Daniel R.; Donis, Ruben O.

CORPORATE SOURCE: Department of Veterinary and Biomedical Sciences, University of Nebraska-Lincoln, Lincoln, NE, 68583-0905, USA

SOURCE: Journal of Virology (2001), 75(17), 8127-8136
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

Influenza A virus expresses three viral polymerase (P) subunits-PB1, PB2, and PA-all of which are essential for RNA and viral replication. The functions of P proteins in transcription and replication have been partially elucidated, yet some of these functions seem to be dependent on the formation of a heterotrimer for optimal viral RNA transcription and replication. Although it is conceivable that heterotrimer subunit interactions may allow a more efficient catalysis, direct evidence of their essentiality for viral replication is lacking. Biochem. studies addressing the mol. anatomy of the P complexes have revealed direct interactions between PB1 and PB2 as well as between PB1 and PA. Previous studies have shown that the N-terminal 48 amino acids of PB1, termed domain α, contain the residues required for binding PA. We report here the refined mapping of the amino acid sequences within this small region of PB1 that are indispensable for binding PA by deletion mutagenesis of PB1 in a two-hybrid assay. Subsequently, we used site-directed mutagenesis to identify the critical amino acid residues of PB1 for interaction with PA in vivo. The first 12 amino acids of PB1 were found to constitute the core of the interaction interface, thus narrowing the previous boundaries of domain α. The role of the minimal PB1 domain α in **influenza** ***virus*** gene expression and genome replication was subsequently analyzed by evaluating the activity of a set of PB1 mutants in a model reporter minigenome system. A strong correlation was observed between a functional PA binding site on PB1 and P activity. **Influenza viruses** bearing mutant PB1 genes were recovered using a plasmid-based **influenza** ***virus*** reverse genetics system. Interestingly, **mutations** that rendered PB1 unable to bind PA were either nonviable or severely growth impaired. These data are consistent with an essential role for the N terminus of PB1 in binding PA, P activity, and virus growth.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:447814 CAPLUS

DOCUMENT NUMBER: 136:129725

TITLE: Pattern of **mutation** in the genome of influenza a virus on adaptation to increased virulence in the mouse lung: identification of functional themes

AUTHOR(S): Brown, E. G.; Liu, H.; Kit, L. Chang; Baird, S.; Nesrallah, M.

CORPORATE SOURCE: Department of Biochemistry, Microbiology, and Immunology, University of Ottawa, Ottawa, ON, K1H 8M5, Can.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(12), 6883-6888
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

The genetic basis for virulence in **influenza virus** is largely unknown. To explore the mutational basis for increased virulence in the lung, the H3N2 prototype clin. isolate, A/HK/1/68, was adapted to the

mouse. Genomic sequencing provided the first demonstration, to our knowledge, that a group of 11 **mutations** can convert an avirulent virus to a virulent variant that can kill at a minimal dose. Thirteen of the 14 amino acid substitutions (93%) detected among clonal isolates were likely instrumental in adaptation because of their pos. selection, location in functional regions, and/or independent occurrence in other virulent ***influenza*** **viruses**. **Mutations** in virulent variants repeatedly involved nuclear localization signals and sites of protein and RNA interaction, implicating them as novel modulators of virulence. Mouse-adapted variants with the same hemagglutinin **mutations** possessed different pH optima of fusion, indicating that fusion activity of hemagglutinin can be modulated by other viral genes. Exptl. adaptation resulted in the selection of three **mutations** that were in common with the virulent human H5N1 isolate A/HK/156/97 and that may be instrumental in its extreme virulence. Anal. of viral adaptation by serial passage appears to provide the identification of biol. relevant **mutations**.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:50834 CAPLUS
DOCUMENT NUMBER: 134:111216
TITLE: Helper virus-free reconstitution of segmented negative-strand RNA viruses using plasmid expression vectors
INVENTOR(S): Brownlee, George Gow; Fodor, Ervin; Palese, Peter; Garcia-Sastre, Adolfo
PATENT ASSIGNEE(S): Isis Innovation Limited, UK; Mount Sinai School of Medicine of New York University
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004333	A1	20010118	WO 2000-GB2710	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194580	A1	20020410	EP 2000-946097	20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003520573	T2	20030708	JP 2001-509537	20000714

PRIORITY APPLN. INFO.:

US 1999-143645P	P	19990714
GB 1999-16794	A	19990716
WO 2000-GB2710	W	20000714

ABSTRACT:
There is disclosed a method for generating in cultured cells infectious viral particles of a segmented neg.-strand virus by an entirely vector-based system without the aid of a helper virus, e.g. by a totally plasmid-based method. The method may, for example, be particularly useful for producing modified ***influenza*** **viruses**. Thus, plasmids for direct expression of the viral RNA segments of an influenza A virus and expression of influenza A nucleoprotein and **RNA-dependent RNA**

polymerase subunits are cotransfected into cultured Vero cells. MDCK cells are employed for plaque assay and amplification of rescued viral particles, although other cells which support growth of influenza A virus may equally be employed. The viral RNA segments provided in the host cells may addnl. or alternatively incorporate one or more attenuating **mutations** . Helper virus-free rescue is particularly favored for generation of reassortant viruses.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:50779 CAPLUS
DOCUMENT NUMBER: 134:114850
TITLE: Production of recombinant respiratory syncytial viruses expressing immune modulatory molecules
INVENTOR(S): Collins, Peter L.; Bukreyev, Alexander; Murphy, Brian R.; Whitehead, Stephen S.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004271	A2	20010118	WO 2000-US19042	20000712
WO 2001004271	A3	20010719		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000062112	A5	20010130	AU 2000-62112	20000712
EP 1194581	A2	20020410	EP 2000-948641	20000712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000013202	A	20020924	BR 2000-13202	20000712
JP 2003512817	T2	20030408	JP 2001-509475	20000712

PRIORITY APPLN. INFO.: US 1999-143425P P 19990713
WO 2000-US19042 W 20000712

ABSTRACT:
Recombinant respiratory syncytial virus (RSV) are provided which express one or more immune modulatory mols. The recombinant virus is modified by addition or substitution of a sequences encoding the immune modulatory mol. (e.g., cytokines). Introduction of a cytokine increases, decreases, or otherwise enhances aspects of viral biol. and/or host immune responses to RSV. In one example, the murine interferon-γ gene was inserted into the RSV G-F intergenic region. Cultured cells infected with rRSV/mIFN-γ expressed the cytokine and replication of the recombinant virus was attenuated in upper and lower respiratory tract of infected mice.

L5 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:539664 CAPLUS
DOCUMENT NUMBER: 134:247761
TITLE: A simple restriction fragment length polymorphism-based strategy that can distinguish the

internal genes of human H1N1, H3N2, and H5N1 influenza A viruses

AUTHOR(S): Cooper, Lynn A.; Subbarao, Kanta

CORPORATE SOURCE: Influenza Branch, Centers for Disease Control and Prevention, Atlanta, GA, 30333, USA

SOURCE: Journal of Clinical Microbiology (2000), 38(7), 2579-2583
CODEN: JCMIDW; ISSN: 0095-1137

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

A simple mol. technique for rapid genotyping was developed to monitor the internal gene composition of currently circulating influenza A viruses. Sequence information from recent H1N1, H3N2, and H5N1 human virus isolates was used to identify conserved regions within each internal gene, and gene-specific PCR primers capable of amplifying all three virus subtypes were designed. Subtyping was based on subtype-specific restriction fragment length polymorphism (RFLP) patterns within the amplified regions. The strategy was tested in a blinded fashion using 10 control viruses of each subtype (total, 30) and was found to be very effective. Once standardized, the genotyping method was used to identify the origin of the internal genes of 51 influenza A viruses isolated from humans in Hong Kong during and immediately following the 1997-1998 H5N1 outbreak. No avian-human or H1-H3 reassortants were detected. Less than 2% (6 of 486) of the RFLP analyses were inconclusive; all were due to point **mutations** within a restriction site. The technique was also used to characterize the internal genes of two avian H9N2 viruses isolated from children in Hong Kong during 1999.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:133841 CAPLUS

DOCUMENT NUMBER: 132:179579

TITLE: Cold-adapted equine **influenza viruses** and reassortants for vaccination of horses

INVENTOR(S): Dowling, Patricia W.; Youngner, Julius S.

PATENT ASSIGNEE(S): University of Pittsburgh-of the Commonwealth System of Higher Education, USA

SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009702	A1	20000224	WO 1999-US18583	19990812
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6177082	B1	20010123	US 1998-133921	19980813
CA 2339089	AA	20000224	CA 1999-2339089	19990812
AU 9954877	A1	20000306	AU 1999-54877	19990812
AU 760356	B2	20030515		

EP 1105497	A1	20010613	EP 1999-941169	19990812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002522078	T2	20020723	JP 2000-565137	19990812
US 6482414	B1	20021119	US 2000-506286	20000216
US 6436408	B1	20020820	US 2000-634159	20000809
US 6579528	B1	20030617	US 2001-762861	20010824
US 2003180322	A1	20030925	US 2002-180633	20020626
US 6649169	B2	20031118		
US 2003199074	A1	20031023	US 2002-65133	20020919
US 6685946	B2	20040203		
US 2004022809	A1	20040205	US 2003-434811	20030508

PRIORITY APPLN. INFO.:

US 1998-133921	A2	19980813
WO 1999-US18583	W	19990812
US 2000-506286	A3	20000216
US 2000-634159	A3	20000809
US 2001-762861	A3	20010824

ABSTRACT:
The present invention provides exptl.-generated cold-adapted equine ***influenza*** **viruses**, and reassortant influenza A viruses comprising at least one genome segment of such an equine **influenza** ***virus*** , wherein the equine **influenza virus** genome segment confers at least one identifying phenotype of the cold-adapted equine ***influenza*** **virus**, such as cold-adaptation, temperature sensitivity, dominant interference, or attenuation. Such viruses are formulated into therapeutic compns. to protect animals from diseases caused by influenza A viruses, and in particular, to protect horses from disease caused by equine ***influenza*** **virus**. The present invention also includes methods to protect animals from diseases caused by influenza A virus utilizing the claimed therapeutic compns. Such methods include using a therapeutic composition as a vaccine to generate a protective immune response in an animal prior to exposure to a virulent virus, and using a therapeutic composition as a treatment for an animal that has been recently infected with a virulent virus, or is likely to be subsequently exposed to virulent virus in a few days whereby the therapeutic composition interferes with the growth of the virulent virus, even in the absence of immunity. The present invention also provides methods to produce cold-adapted equine **influenza viruses**, and reassortant influenza A viruses having at least one genome segment of an equine ***influenza*** **virus** generated by cold-adaptation. Nucleotide and protein sequences are provided for wild-type and cold-adapted RNA segments encoding the matrix (M), hemagglutinin (HA), and **RNA**-***dependent*** **RNA polymerase** (N-terminal and C-terminal portions).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:223017 CAPLUS
DOCUMENT NUMBER:	130:263124
TITLE:	attenuated recombinant respiratory syncytial virus expression systems and vaccines
INVENTOR(S):	Jin, Hong; Tang, Roderick; Li, Shengqiang; Bryant, Marty
PATENT ASSIGNEE(S):	Aviron, USA
SOURCE:	PCT Int. Appl., 85 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9915631 A1 19990401 WO 1998-US20230 19980928

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003054505	A1	20030320	US 1998-161122	19980925
CA 2304932	AA	19990401	CA 1998-2304932	19980928
AU 9895852	A1	19990412	AU 1998-95852	19980928
EP 1017791	A1	20000712	EP 1998-949553	19980928

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

US 2003027321	A1	20030206	US 2001-923070	20010806

PRIORITY APPLN. INFO.:

US 1997-60153P	P	19970926
US 1998-84133P	P	19980504
US 1998-89207P	P	19980612
US 1997-69153P	P	19971209
US 1998-161122	A1	19980925
WO 1998-US20230	W	19980928

ABSTRACT:
The present invention relates to genetically engineered recombinant RS viruses and viral vectors which contain heterologous genes for use as vaccines. In accordance with the present invention, the recombinant RS viral vectors and viruses are engineered to contain heterologous genes, including genes of other viruses, pathogens, cellular genes, tumor antigens, or to encode combinations of genes from different strains of RSV.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:395600 CAPLUS
DOCUMENT NUMBER: 129:106391
TITLE: **Influenza virus** nucleoprotein interacts with **influenza virus** polymerase proteins
AUTHOR(S): Biswas, Siddhartha K.; Boutz, Paul L.; Nayak, Debi P.
CORPORATE SOURCE: Department of Microbiology and Immunology, Jonsson Comprehensive Cancer Center, UCLA School of Medicine, Los Angeles, CA, 90095-1747, USA
SOURCE: Journal of Virology (1998), 72(7), 5493-5501
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
Influenza virus nucleoprotein (NP) is a critical factor in the viral infectious cycle in switching **influenza virus** RNA synthesis from transcription mode to replication mode. In this study, we investigated the interaction of NP with the viral polymerase protein complex. Using coimmunopptn. with monospecific or monoclonal antibodies, we observed that NP interacted with the RNP-free polymerase protein complex in **influenza** ***virus*** -infected cells. In addn., coexpression of the components of the polymerase protein complex (PB1, PB2, or PA) with NP either together or pairwise revealed that NP interacts with PB1 and PB2 but not PA. Interaction of NP with PB1 and PB2 was confirmed by both coimmunopptn. and histidine tagging of the NP-PB1 and NP-PB2 complexes. Further, it was obsd. that NP-PB2 interaction was rather labile and sensitive to dissocn. in 0.1% sodium dodecyl sulfate and that the stability of NP-PB2 interaction was regulated by the sequences present at the COOH terminus of NP. Anal. of NP deletion mutants revealed that at least three regions of NP interacted independently with PB2.

A detailed anal. of the COOH terminus of NP by **mutation** of serine-to-alanine (SA) residues either individually or together demonstrated that SA **mutations** in this region did not affect the binding of NP to PB2. However, some SA **mutations** at the COOH terminus drastically affected the functional activity of NP in an in vivo transcription-replication assay, whereas others exhibited a temp.-sensitive phenotype and still others had no effect on the transcription and replication of the viral RNA. These results suggest that a direct interaction of NP with polymerase proteins may be involved in regulating the switch of viral RNA synthesis from transcription to replication.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:467533 CAPLUS
DOCUMENT NUMBER: 125:163040
TITLE: Mutational analysis of the **influenza virus** A/Victoria/3/75 PA protein: studies of interaction with PB1 protein and identification of a dominant negative mutant
AUTHOR(S): Zurcher, Thomas; de la Luna, Susana; Sanz-Ezquerro, Juan J.; Nieto, Amelia; Ortin, Juan
CORPORATE SOURCE: Centro Nactional Biotecnologia, Universidad Autonoma, Madrid, 28049, Spain
SOURCE: Journal of General Virology (1996), 77(8), 1745-1749
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The RNA polymerase activity and PB1 binding of **influenza** ***virus*** PA mutants were studied using an in vivo-reconstituted polymerase assay and a two hybrid system. Deletions covering the whole PA protein abolished polymerase activity, but the deletion of the 154 N-terminal amino acids allowed PB1 binding, indicating that the PA protein N terminus is not absolutely required for this interaction. Further internal or C-terminal deletions abolished PB1 interaction, suggesting that most of the protein is involved in this association As a novel finding we showed that a single amino acid insertion mutant, PAI672, was responsible for a temperature-sensitive phenotype. Mutant PAS509, which had a serine insertion at position 509, bound to PB1 like wild-type PA but did not show any polymerase activity. Over-expression of PAS509 interfered with the polymerase activity of wild-type PA, identifying PAS509 as a dominant neg. mutant.

L5 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:379959 CAPLUS
DOCUMENT NUMBER: 125:27697
TITLE: Chimeric **influenza virus** for recombinant ribonucleoprotein, M protein, or NP protein expression and electroporation for animal cell culture transfection
INVENTOR(S): Li, Shenqiang; Coelingh, Kathleen Louise; Palese, Peter M.
PATENT ASSIGNEE(S): Aviron, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9610633	A1	19960411	WO 1995-US12559	19950929	
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9537604	A1	19960426	AU 1995-37604	19950929	
PRIORITY APPLN. INFO.:			US 1994-316049	19940930	
			WO 1995-US12559	19950929	

ABSTRACT:
A method for producing chimeric **influenza virus** comprising transfection of a host cell with a recombinant ribonucleoprotein by electroporation and infection with a parental strain of influenza is described. Transfection of a host cell with a recombinant ribonucleoprotein by electroporation for recombinant gene expression is also described. Chimeric ***influenza*** **viruses** comprising heterologous influenza M protein coding sequence, or comprising heterologous influenza NP coding sequence, are also described. The heterologous influenza coding sequence may contain at least one substitution of a native residue with a non-native residue.

L5 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1995:676963 CAPLUS
DOCUMENT NUMBER:	123:104224
TITLE:	The choice of alternative 5' splice sites in **influenza virus** M1 mRNA is regulated by the viral polymerase complex
AUTHOR(S):	Shih, Shin-Ru; Nemeroff, Martin E.; Krug, Robert M.
CORPORATE SOURCE:	Dep. Mol. Biol. Biochem., Rutgers Univ., Piscataway, NJ, 08855-1179, USA
SOURCE:	Proceedings of the National Academy of Sciences of the United States of America (1995), 92(14), 6324-8 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:	National Academy of Sciences
DOCUMENT TYPE:	Journal
LANGUAGE:	English

ABSTRACT:
The **influenza virus** M1 mRNA has two alternative 5' splice sites: a distal 5' splice site producing mRNA3 that has the coding potential for 9 amino acids and a proximal 5' splice site producing M2 mRNA encoding the essential M2 ion-channel protein. Only mRNA3 was made in uninfected cells transfected with DNA expressing M1 mRNA. Similarly, using nuclear exts. from uninfected cells, in vitro splicing of M1 mRNA yielded only mRNA3. Only when the mRNA3 5' splice site was inactivated by **mutation** was M2 mRNA made in uninfected cells and in uninfected cell exts. In **influenza** ***virus*** -infected cells, M2 mRNA was made, but only after a delay, suggesting that newly synthesized viral gene product(s) were needed to activate the M2 5' splice site. We present strong evidence that these gene products are the complex of the three polymerase proteins, the same complex that functions in the transcription and replication of the viral genome. Gel shift expts. showed that the viral polymerase complex bound to the 5' end of the viral M1 mRNA in a sequence-specific and cap-dependent manner. During in vitro splicing catalyzed by uninfected cell exts., the binding of the viral polymerase complex blocked the mRNA3 5' splice site, resulting in the switch to the M2 mRNA 5' splice site and the production of M2 mRNA.

L5 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1995:218571 CAPLUS
DOCUMENT NUMBER:	122:51059
TITLE:	Evaluation of the genetic stability of the

temperature-sensitive PB2 gene **mutation** of the influenza A/Ann Arbor/6/60 cold-adapted vaccine virus

AUTHOR(S): Treanor, John; Perkins, Mark; Battaglia, Rosalyn; Murphy, Brian R.

CORPORATE SOURCE: Laboratory Infectious Diseases, National Institute Allergy and Infectious Diseases, Bethesda, MD, 20892, USA

SOURCE: Journal of Virology (1994), 68(12), 7684-8
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

ABSTRACT:

A single-gene reassortant bearing the PB2 gene of the A/Ann Arbor/6/60 cold-adapted virus in the background of the A/Korea/82 (H3N2) wild-type virus is a temperature-sensitive (ts) virus with an in vitro shutoff temperature of 38°. A single **mutation** at amino acid (aa) at 265 (asp-Ser) of the PB2 protein is responsible for the ts phenotype. This ts single-gene PB2 reassortant virus was serially passaged at elevated temps. in Madin-Darby canine kidney cells to generate ts+ phenotypic revertant viruses. Four ts+ phenotypically revertant viruses were derived independently, and each possessed a shutoff temperature for replication in vitro of >40°. Each of the four phenotypically revertant viruses replicated efficiently in the upper and lower respiratory tracts of mice and hamsters, unlike the PB2 single-gene reassortant virus, confirming that the ts phenotype was responsible for the attenuation of this virus in rodents. Mating the ts+ revertants with wild-type virus yielded ts progeny in high frequency, indicating that the loss of ts phenotype was due to a suppressor **mutation** which was mapped to the PA gene in each of the four independently derived ts phenotypic revertants. Nucleotide sequence anal. confirmed the absence of new **mutations** on the PB2 gene and the presence of predicted amino acid changes in the PA proteins of the revertant viruses. These studies suggest that single amino acid changes at aa 245 (Glu-Lys) or 347 (Asp-Asn) of the PA protein can completely suppress the ts and attenuation phenotypes specified by the Asp-Ser **mutation** at aa 265 of the PB2 protein of the A/Ann Arbor 6/60 cold-adapted virus.

L5 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:50027 CAPLUS

DOCUMENT NUMBER: 120:50027

TITLE: Attenuation of segmented RNA viruses by by modification of the genomic RNA

INVENTOR(S): Palese, Peter

PATENT ASSIGNEE(S): Mount Sinai School of Medicine, USA

SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321306	A1	19931028	WO 1993-US3615	19930413
W: AU, BB, BG, BR, CA, CZ, FI, GB, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9302588	A	19931102	ZA 1993-2588	19930413
AU 9342893	A1	19931118	AU 1993-42893	19930413
AU 687738	B2	19980305		
EP 636172	A1	19950201	EP 1993-912288	19930413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

CN 1082606	A	19940223	CN 1993-105933		19930414
CN 1065912	B	20010516			
US 6022726	A	20000208	US 1994-318794		19941220
US 6316243	B1	20011113	US 1995-470106		19950606
PRIORITY APPLN. INFO.:			US 1992-868596	A2	19920414
			US 1992-841310	B3	19920203
			US 1992-938975	B2	19920901
			WO 1993-US3615	A	19930413
			US 1994-318794	A3	19941220

ABSTRACT:
Segmented RNA viruses are attenuated by alteration of the noncoding or coding sequence of a gene. Alterations of noncoding regions which regulate transcription or replication result in down-regulation of the viral gene and an attenuation of the virus, either by production of defective particles during replication or by reducing the number of progeny virions produced during viral replication. Anal. of the mechanism of attenuation of the transfectant ***influenza*** **virus** NA/B-NS indicated that reduced efficiency of replication of the chimeric NA gene was due to alteration of cis elements and so was responsible for attenuation. This cis element alteration resulted in a higher proportion of defective particles than in wild type virus prepns. An ***influenza*** **virus** containing a chimeric gene for hemagglutinin into which the ME1 epitope of Plasmodium yoelii was inserted was prepared When assayed in mice, this chimeric virus had a 500-1000-fold higher LD50 than the wild type virus.

L5 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1993:74689 CAPLUS
DOCUMENT NUMBER:	118:74689
TITLE:	Nucleotides 9 to 11 of the influenza A virion RNA promoter are crucial for activity in vitro
AUTHOR(S):	Seong, B. L.; Brownlee, G. G.
CORPORATE SOURCE:	Sir William Dunn Sch. Pathol., Univ. Oxford, Oxford, OX1 3RE, UK
SOURCE:	Journal of General Virology (1992), 73(12), 3115-24 CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE:	Journal
LANGUAGE:	English

ABSTRACT:
The 12 nucleotide conserved sequence at the 3' end of influenza A virion RNA is sufficient to function as a promoter in vitro. By introducing point ***mutations*** in all 12 positions of this promoter in model RNA templates and studying the efficiency of RNA synthesis in vitro, it is shown that only three nucleotides, residues 9, 10 ad 11, are crucial for activity, although other nucleotides play a significant but less important role. Addns. or deletions within the promoter are tolerated, resulting in either an increase or a decrease in promoter activity, depending on the **mutation** introduced; in some cases premature termination is caused. Taking these observations into account, a model for RNA polymerase binding and copying of the promoter is discussed.

L5 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1990:527335 CAPLUS
DOCUMENT NUMBER:	113:127335
TITLE:	**Mutation** in NS2, a nonstructural protein of influenza A virus, extragenically causes aberrant replication and expression of the PA gene and leads to generation of defective interfering particles
AUTHOR(S):	Odagiri, Takato; Tobita, Kiyotake
CORPORATE SOURCE:	Dep. Virol., Jichi Med. Sch., Minami Kawachi, 329-04, Japan
SOURCE:	Proceedings of the National Academy of Sciences of the United States of America (1990), 87(15), 5988-92

CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Several consecutive undiluted passages of infectious virus are usually required to obtain defective interfering particles of **influenza virus**. In contrast, a reassortant (Wa-182) of influenza A/WSN, whose NS gene was replaced with the NS gene of A/Aichi, was readily converted to defective interfering from after only a single high-multiplicity infection. The defective interfering particles of Wa-182 were devoid of the PA gene (RNA segment 3) but possessed several species of subgenomic RNAs of the PA gene origin. Such aberrant replication of the PA gene was shown to be caused by an extragenic effect of the NS gene of Wa-182, because, when the NS gene of Wa-182 was singly transferred to the wild-type A/Ann Arbor/6/60 virus, the recipient showed exactly the same features. Anal. of nucleotide sequence demonstrated that the NS gene of Wa-182 contained 3 point **mutations** relative to the wild-type NS gene that resulted in 2 amino acid substitutions in the nonstructural protein NS2, suggesting that the **mutation** in NS2 protein affected the normal replication of the PA gene of Wa-182. The results also suggest that the NS2 protein plays an important role in the synthesis of intact genome RNAs.

L5 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:509816 CAPLUS
DOCUMENT NUMBER: 111:109816
TITLE: Identification of sequence changes in the cold-adapted, live attenuated influenza vaccine strain, A/Ann Arbor/6/60 (H2N2)
AUTHOR(S): Cox, Nancy J.; Kitame, Fumio; Kendal, Alan P.; Maassab, Hunein F.; Naeve, Clayton
CORPORATE SOURCE: Div. Viral Dis., Cent. Infect. Dis., Atlanta, GA, 30333, USA
SOURCE: Virology (1988), 167(2), 554-67
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Nucleotide sequences were obtained for RNA segments encoding the PB2, PB1, PA, NP, M1, M2, NS1, and NS2 proteins of the influenza A/Ann Arbor/6/60 (H2N2) wild-type virus and its cold-adapted derivative that has been used for preparing investigational live attenuated vaccines. Twenty-four nucleotide differences between the cold-adapted and wild type viruses were detected, of which 11 were deduced to code for amino acid substitutions in the cold-adapted virus proteins. One amino acid substitution each was predicted for the PB2, M2, and NS1 proteins. Two amino acid substitutions were predicted for the NP and the PA proteins. Four substitutions were predicted for the PB1 protein. The biol. significance of **mutations** in the PB2, PB1, PA, and M2 genes of the cold-adapted virus is suggested by currently available genetic data, a comparison with other available influenza gene sequences, and the nature of the predicted amino acid changes. In addn., the sequence data confirm the close evolutionary relationship between the genomes of influenza A (H2N2) and influenza A (H3N2) viruses.

L5 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:219875 CAPLUS
DOCUMENT NUMBER: 104:219875
TITLE: Biological characteristics of a cold-adapted influenza A virus **mutation** residing on a polymerase gene
AUTHOR(S): Odagiri, T.; Tosaka, A.; Ishida, N.; Maassab, H. F.
CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, 329-04, Japan
SOURCE: Archives of Virology (1986), 88(1-2), 91-104

CODEN: ARVIDF; ISSN: 0304-8608
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The biol. function of a cold-adapted (ca) **mutation** residing on the ***RNA*** -**dependent RNA polymerase** [9026-28-2] gene PB2 of an influenza A/Ann Arbor/6/60 (A/AA/6/60) ca variant virus in the viral replication cycle at 25° was studied. The viral polypeptide synthesis of A/AA/6/60 ca variant at 25° was evident .apprx.6 h earlier than was the wild-type (wt) virus and yielded twice as many products. The quant. anal. of viral complementary RNA (cRNA), synthesized in the presence of cycloheximide, revealed that the A/AA/6/60 ca variant and a single gene reassortment that contains only the PB2 gene of the ca variant with remaining genes of the wt virus produced equal amts. of cRNA at 25° and 33°, which was an amount .apprx.4-fold greater than the wt virus' cRNA synthesized at 25°. These results strongly suggest that the ca ***mutation*** residing on the PB2 gene of A/AA/6/60 ca variant affects mRNA synthesis at 25° in primary transcription.

L5 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:205587 CAPLUS
DOCUMENT NUMBER: 100:205587
TITLE: Capped mRNAs may stimulate the influenza virion polymerase by allosteric modulation
AUTHOR(S): Penn, Charles R.; Mahy, Brian W. J.
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Virus Research (1984), 1(1), 1-13
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Analogs of the mRNA 5'-terminal Me cap structure stimulated the influenza virion **RNA-dependent RNA polymerase**.
The single nucleotide analog m7GMP was incorporated into RNA during transcription in vitro, and the stimulatory effect was not additive with the primer ApG, suggesting that m7GMP stimulates the virion polymerase by priming virus-specific mRNA synthesis, as has been shown for ApG. By contrast, stimulation by m7G(5')ppp(5')m6Am2-O was additive with that by ApG, and incorporation of the similar analog m7G(5')ppp(5')Am2-O into RNA during transcription could not be demonstrated. Apparently, these dinucleotide cap analogs stimulate the virion polymerase by allosteric modulation, independent of priming. This stimulation can be abolished by **mutation**, without loss of other activities associated with the cap-dependent endonuclease.

=> DIS L4 1- IBIB IABS
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):Y
THE ESTIMATED COST FOR THIS REQUEST IS 7.62 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:634334 CAPLUS
DOCUMENT NUMBER: 137:180775
TITLE: **Influenza viruses** with enhanced transcription and replication capacities comprising RNA polymerase similar to that of fowl plague virus and uses for gene therapy and vaccination
INVENTOR(S): Hobom, Gerd; Menke, Anette
PATENT ASSIGNEE(S): Artemis Pharmaceuticals Gmbh, Germany
SOURCE: Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1233059	A1	20020821	EP 2001-103060	20010209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002064757	A2	20020822	WO 2002-EP1257	20020207
WO 2002064757	A3	20021205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368459	A2	20031210	EP 2002-716735	20020207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003099670	A1	20030529	US 2002-73377	20020208

PRIORITY APPLN. INFO.:			
EP 2001-103060	A	20010209	
US 2001-270135P	P	20010220	
WO 2002-EP1257	W	20020207	

ABSTRACT:
The present invention provides human **influenza viruses** comprising an RNA sequence encoding a modified RNA-polymerase (RNAP). It was found that specific **modifications** of the RNA sequence encoding the RNAP, in particular the RNAP PB1 subunit - so as to code for a polypeptide having a higher similarity with fowl plague virus strain Bratislava (FPV) RNAP - provides viruses capable of recognition of viral RNA (vRNA) promoter sequence variations (the so called promoter-up variants) leading to an increase in transcription and/or replication initiation rates. The vRNA promoter may comprise the **modifications** G3A and C8U, or G3C and C8G, preferably G3A, U5C and C8U, or G3C, U5C and C8G in the 3'-terminal region (5'-CCUGUUUCUACU-3' or 5'-CCUGUUUUUACU-3'); and the **modifications** U3A and A8U in the 5'-terminal region (5'-AGAAGAAUCAAGG-3'). The present invention also provides a process for the preparation thereof, pharmaceutical compns. comprising said human **influenza viruses** and their use for gene transfer into mammalian cells, for ex vivo gene transfer into antigen-presenting cells, such as dendritic cells, for in vivo somatic gene therapy, or in vivo vaccination purposes. The invention also relates to other non-avian **influenza viruses**, including equine, porcine ***influenza*** **viruses**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:50779 CAPLUS
DOCUMENT NUMBER: 134:114850
TITLE: Production of recombinant respiratory syncytial viruses expressing immune modulatory molecules
INVENTOR(S): Collins, Peter L.; Bukreyev, Alexander; Murphy, Brian R.; Whitehead, Stephen S.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004271	A2	20010118	WO 2000-US19042	20000712
WO 2001004271	A3	20010719		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000062112	A5	20010130	AU 2000-62112	20000712
EP 1194581	A2	20020410	EP 2000-948641	20000712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000013202	A	20020924	BR 2000-13202	20000712
JP 2003512817	T2	20030408	JP 2001-509475	20000712

PRIORITY APPLN. INFO.:	US 1999-143425P	P	19990713
	WO 2000-US19042	W	20000712

ABSTRACT:
Recombinant respiratory syncytial virus (RSV) are provided which express one or more immune modulatory mols. The recombinant virus is modified by addition or substitution of a sequences encoding the immune modulatory mol. (e.g., cytokines). Introduction of a cytokine increases, decreases, or otherwise enhances aspects of viral biol. and/or host immune responses to RSV. In one example, the murine interferon-γ gene was inserted into the RSV G-F intergenic region. Cultured cells infected with rRSV/mIFN-γ expressed the cytokine and replication of the recombinant virus was attenuated in upper and lower respiratory tract of infected mice.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1994:50027 CAPLUS
DOCUMENT NUMBER:	120:50027
TITLE:	Attenuation of segmented RNA viruses by by **modification** of the genomic RNA
INVENTOR(S):	Palese, Peter
PATENT ASSIGNEE(S):	Mount Sinai School of Medicine, USA
SOURCE:	PCT Int. Appl., 71 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321306	A1	19931028	WO 1993-US3615	19930413
W: AU, BB, BG, BR, CA, CZ, FI, GB, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9302588	A	19931102	ZA 1993-2588	19930413
AU 9342893	A1	19931118	AU 1993-42893	19930413
AU 687738	B2	19980305		
EP 636172	A1	19950201	EP 1993-912288	19930413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1082606	A	19940223	CN 1993-105933	19930414
CN 1065912	B	20010516		
US 6022726	A	20000208	US 1994-318794	19941220

US 6316243	B1	20011113	US 1995-470106		19950606
PRIORITY APPLN. INFO.:			US 1992-868596	A2	19920414
			US 1992-841310	B3	19920203
			US 1992-938975	B2	19920901
			WO 1993-US3615	A	19930413
			US 1994-318794	A3	19941220

ABSTRACT:
Segmented RNA viruses are attenuated by alteration of the noncoding or coding sequence of a gene. Alterations of noncoding regions which regulate transcription or replication result in down-regulation of the viral gene and an attenuation of the virus, either by production of defective particles during replication or by reducing the number of progeny virions produced during viral replication. Anal. of the mechanism of attenuation of the transfectant ***influenza*** **virus** NA/B-NS indicated that reduced efficiency of replication of the chimeric NA gene was due to alteration of cis elements and so was responsible for attenuation. This cis element alteration resulted in a higher proportion of defective particles than in wild type virus prepns. An ***influenza*** **virus** containing a chimeric gene for hemagglutinin into which the ME1 epitope of Plasmodium yoelii was inserted was prepared When assayed in mice, this chimeric virus had a 500-1000-fold higher LD50 than the wild type virus.

=> L4 and mutation
L9 3 L4 AND MUTATION

=> L4 and modification
L10 0 L4 AND MODIFICATION

=> D L9 IBIB TI SO AU ABS 1-3

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:56467 CAPLUS
DOCUMENT NUMBER: 114:56467
TITLE: The critical cut-off temperature of avian influenza viruses
AUTHOR(S): McCauley, John W.; Penn, Charles R.
CORPORATE SOURCE: Inst. Anim. Health, AFRC, Surrey, GU24 0NF, UK
SOURCE: Virus Research (1990), 17(3), 191-8
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English
TI The critical cut-off temperature of avian influenza viruses
SO Virus Research (1990), 17(3), 191-8
CODEN: VIREDF; ISSN: 0168-1702
AU McCauley, John W.; Penn, Charles R.
AB The pathogenicity of H7 avian influenza viruses for 6-wk-old chicks was measured. One virus, strain S3 from A/**FPV**/Rostock/34(H7N1) showed a temperature sensitive phenotype at 41.5° and reduced pathogenicity. By anal. of reassortants made between virus S3 and A/**FPV**/Dobson/27(**H7N7**), a fully pathogenic virus, 2 conclusions arise. (1) The critical cut-off temperature for avian influenza virus in 6-wk-old chicks is 41.5°. (2) RNA segment 1 of virus S3 is responsible for the lack of pathogenicity in reassortant viruses. Nucleotide sequencing of RNA segment 1 from S3 and its parent, A/**FPV**/Rostock/34 has revealed a single **mutation** at nucleotide 1561. This results in a substitution of isoleucine for leucine at amino acid position 512 in the cap-binding protein, PB2.

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=> "recombinant influenza virus"
L1          188 "RECOMBINANT INFLUENZA VIRUS"

=> "flow plague virus"
L2            1 "FLOW PLAGUE VIRUS"

=> FPV
L3          845 FPV

=> H7N7 and L3
L4           31 H7N7 AND L3

=> human and L1
L5           77 HUMAN AND L1

=> L5 and L4
L6            1 L5 AND L4

=> "avian influenza virus"
L7          985 "AVIAN INFLUENZA VIRUS"

=> L7 and L5
L8            2 L7 AND L5

=> D L8 IBIB TI SO AU ABS 1-2
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